

1 GAATTCAGGCTGCTAGGAAGTGAAGTGAACCTGGACCCAGCTCAGCGGCAGCAGCAG 60

61 CCGCAGCAGGCAGCAGCCTCTATCCTCTCCTCCAGCCACATGGGCCCCGGATGGCGCTT 120
MetGlyProArgMetAlaLeu

121 CCCCCGCTGCTCCTGCTCCTGTTCTTGCACCTGTTGCTGCTAGGATGCCGTTCCCATCCA 180
ProArgValLeuLeuLeuLeuPheLeuHisLeuLeuLeuGlyCysArgSerHisPro
eProAlaCysSerCysSerCysThrCysCysCysEndAspAlaValProIleHi
erProArgAlaProAlaProValLeuAlaProValAlaAlaArgMetProPheProSerT

181 CTGGGTGGCGCTGGCCTGCCTCAGAACTGCCAGGGATACAGGTGAGCCCTGATGAACCTG 240
LeuGlyGlyAlaGlyLeuAlaSerGluLeuProGlyIleGlnValSerProAspGluLeu
sTrpValAlaLeuAlaTrpProGlnAsnCysGlnGlyTyrArgEndAlaLeuMetAsnCy
hrGlyTrpArgTrpProGlyLeuArgThrAlaArgAspThrGlyGluProEndEndThra

241 CTAGACTTGGTGGCTGGAGGGCGGACAGCAGCAACTAACGGGTCCCCACCTACTG 300
LeuArgLeuGlyTrpLeuGlyGlyArgGlyGlnGlnGlnLeuThrGlyProHisLeuLeu
sLeuAspLeuValGlyTrpGluGlyAlaAspSerSerAsnEndArgValProThrTyrCy
laEndThrTrpLeuAlaGlyArgAlaArgThrAlaAlaThrAsnGlySerProProThrV

FIG.1A

301 TTCCAAGAGGGCTCTAACCTCCTTTGGAACTAGTGATAAGGGGTTTAGAAGGCAGCCAG 360
 PheGlnGluGlySerAsnLeuLeuTrpGluLeuValIleArgGlyLeuGluGlySerGln
 sSerLysArgAlaLeuThrSerPheGlyAsnEndEndGlyValEndLysAlaAlaAr
 alProArgGlyLeuEndProProLeuGlyThrSerAspLysGlyPheArgArgGlnProG

361 GCTGGGGGTGAGGACCCGCTCCCAAGGCAGTTGGTTCGCTTCAGCACCATCAAGAGTGAT 420
 AlaGlyGlyGluAspProLeuProArgGlnLeuValArgPheSerThrIleLysSerAsp
 gLeuGlyValArgThrArgSerGlnGlySerTrpPheAlaSerAlaProSerArgValMe
 lyTrpGlyEndGlyProAlaProLysAlaValGlySerLeuGlnHisGlnGluEndT

421 GGTCCAGGTGGAGTTCCTGAGGCTCGGGCTCCCCACCCATCCAGGAGCTGCTGGAC 480
 GlySerArgCysGluPheLeuArgLeuGlyLeuProHisProSerGlnGluLeuAsp
 tGlyProGlyAlaSerSerEndGlySerGlySerProThrHisProArgSerCysTrpTh
 rpValGlnValArgValProGluAlaArgAlaProProIleProGlyAlaAlaGlyP

481 CGCCTGGCAGACAGGGTCTCCGAGCTGCAGGCGACGGACGGACCTGGAGCCCTCCGGC 540
 ArgLeuArgAspArgValSerGluLeuGlnAlaThrGlyArgThrTrpSerProSerGly
 rAlaCysGluThrGlySerProSerCysArgArgArgAspGlyProGlyAlaProProAl
 roProAlaArgGlnGlyLeuArgAlaAlaGlyAspGlyThrAspLeuGluProLeuArgG

541 AGGACCGTGGCCTCACAGAAGCCTGGAGGCGGAGGAGCAGCCCCACGGGGTCTTG 600
 ArgThrValAlaSerGlnLysProGlyArgArgGlyLysGlnProProArgGlyPheLeu
 aGlyProTrpProHisArgSerLeuGlyGlyGluGlySerSerProHisGlyGlySerTr
 lNaspArgGlyLeuThrGluAlaTrpGluAlaArgGluAlaAlaProThrGlyValLeuG

FIG.1B

601 GCGCCCGCAGTAGCATCTTCCAAGTCTCTCGGGGAATACGCAGCCCCAAGACGATGCGTG 660
 GlyProAlaValAlaSerSerLysSerSer
 pAlaProGlnEndHisLeuProSerProPro
 lyProArgSerSerIlePheGlnValLeuArgGlyIleArgSerProLysThrMetArgA

661 ACTCTGGCTGCTTTGGGGGAGGCTGGACCGGATCGGCTCCCTCAGCGGCCTGGGCTGCA 720
spSerGlyCysPheGlyArgArgLeuAspArgIleGlySerLeuSerGlyLeuGlyCysA

721 ATGGTGAGCACCCACCCCAATTCCCACCTGCACGCCCGGTTAGCATCACTTCTGGGTTTGA 780
snV

781 TGTCTCTGGGACCAAACTCCGAGAAAGGACACCTGGATAATCACTCTTTCTTGTGCCAG 840

841 TCCTCAAGGCCAAGGAGCGCCTTCTCGCCACCCCTGCCTCTCTCACCCAAGCGGCAGAT 900

901 GACTATGAGTCCCCACCCACCTTCTCGCCACCCCTGCCTCTCTCACCCAAGCGGCAGAT 960

961 ATTACTTTAGGATGTAAATTCTGTCAATTGCCCTGGCTGCCGCTCCTGGGAGCAAAAAGAGA 1020

FIG.1C

1021 ACTAACCTCTTCCCCCTGGTTTCCCCCTCAACTGTCTGTGGCTGCAAGGCAGAGGGCAG 1080
 1081 GATCACCAGGGTGATGACAAGTCCCAGCTTACAAGGAGGAAACTCAGGTCCAGAGAGATG 1140
 1141 GATTATCCCAAGCCCCCAACATCCAGTTCTGCTGAAGAAGCGGGTGGCAGGGTGGCA 1200
 1201 CGTGGTGGGGGAAGCCAGGTCCTGCCTGCCTCTCACCCCTAATGTCACTCACCCCTCT 1260
 1261 CTCTCCCCCCACAGTGCTCAGGAGGTACTGAGAAGTCTCTGGCTGACAACTCTGTGTCC 1320
 alLeuArgArgTyr**
 1321 GCTTCTCCAAGCCCTCCCTGCTCCCTTCAAAGCAACTCCTGTTTTTATTATGTAT 1380
 1381 TTATTTATTATTATTGGTGTGTATATAAGACGGTTCTTATTGTGAGCACATTTT 1440
 1441 TTCCATGGTGAATAAAGTCAACATTAGAGCTCTGTCTTTTGAAAAAAGGGA 1500

1501 ATTC 1504

FIG.1D

BNP Screening Oligos

5'-TCCAGCTGCTTCGGGGCAGGATGGACAGGATTGGAGCCCAGAGCGGACTGGGCTGTAAAC-3'	human ANP
SerSerCysPheGlyGlyArgMetAspArgIleGlyAlaGlnSerGlyLeuGlyCysAsn-3'	human ANP
(21)	
SerGlyCysPheGlyArgArgLeuAspArgIleGlySerLeuSerGlyLeuGlyCysAsn	pig BNP
5'-ACNGGNTGCTTGGGNCGNCGNCCTNGACCGNATNGGNTCNCNTCTCNGGNCCTNGGNTGCCAAC-3'	Pig BNP
TG T A A A T TA AG T AG T T T	
3'-AGGCCGACGAAGCCCGGTCCGACCTGTCTTAACCTAGGGACTCGCCCTGACCCGACATTG-5'	3351 (min:mal)
3'-TCGCCGACGAAGCCCGTCTTCTGAGCTGTCTTAGCCGTGGAGTCGCCGGAGCCGACGTTG-5'	3352 (G/T pref)
3'-AGGTGACGAAGCCCGTCTTCTGAGCTGTCTTAACCTCGGGTCTCGCCCTGACCCGACATTG-5'	3376 (ANP)

FIG.2

hn BNP cDNA (10-13-88)

```

1  GAATTCAGGCTGCTAGGAAGTGAAGTGAACCTGGACCCAGCTCAGCGGCAGCAGCGGCAGCAGG 70
71  CAGCAGCCTCTATCCTCTCCAGCCACATGGGCCCGGATGGCGCTTCCCCGGCTGCTCCTGCTCCT 140
    MetGlyProArgMetAlaLeuProArgValLeuLeuLeuLe
    └─┬─┘
141  GTTCTTGACACCTGTTGCTGCTAGGATGCCGTTCCCATCCACTGGGTGGCGCTGGCCTCAGAACTG 210
    uPheLeuHisLeuLeuLeuGlyCysArgSerHisProLeuGlyGlyAlaGlyLeuAlaSerGluLeu
    . -1 +1 . 10
211  CCAGGGATACAGGTGAGCCCTGATGAACCTGCTTAGACTTGGTTGGCTGGGAGGCGGACAGCAGCAAC 280
    ProGlyIleGln

281  TAACGGGTCCCCACCTACTGTTCCAAGAGGGCTCTACCTCCTTTGGGAACTAGTGATAAGGGTTAGAA 350
351  GGCAGCCAGGCTGGGGGTGAGGACCCCGCTCCCAAGGCAGTTGGTTGCTTCAGCACCATCAAGAGTGAT 420
421  GGGTCCAGGTGCGAGTTCCTGAGGCTCGGGCTCCCCACCCATCCACGAGAGCTGCTGGACCGCCTGCGAG 490
    GluLeuLeuAspArgLeuArg
    20.
491  ACAGGTCTCCGAGCTGCAGGCGGAGCGGACGACCTGGAGCCCTCCGGCAGGACCGTGGCCTCACAGA 560
    spArgValSerGluLeuGlnAlaGluArgThrAspLeuGluProLeuArgGlnAspArgGlyLeuThrGln
    30. 40.
561  AGCCTGGGAGCGGAGGAGAGCAGCCCCACGGGGTCTTTGGGCCCGCAGTAGCATCTTCCAAGTCCTC 630
    uAlaTrpGluAlaArgGluAlaAlaProThrGlyValLeuGlyProArgSerIlePheGlnValLeu

```

FIG.3A

50. 60. 70.
 631 C G G G A A T A C G C A G C C C A A G A C G A T G C G T G A C T C T G G C T G C T T T G G G G A G G C T G G A C C G G A T C G G C T 700
 Arg Gly Ile Arg Ser Pro Lys Thr Met Arg Asp Ser Gly Cys Phe Gly Arg Arg Leu Asp Arg Ile Gly
 80. 90.
 701 C C C T A G C G G C C T G G G C T G C A A T G T G A G C A C C C A C C C C C A T T C C C A C T G C A G C C C C G G T T A G C A T C A C 770
 er Leu Ser Gly Leu Gly Cys Asn V
 100
 771 T T C T G G G T T T G A T G T C T C T G G G G A C C A A A C T C G G A G A A A G G A C A C C T G G A T A T C A C T C T T C T T G T T G C 840
 841 C A G T C C T C A A G G C C A A G G A G C G C C T T C C T G G A A A A T T A A A T T T G G A C A G C A T T C A C T A G C A T G A C T A T G 910
 911 A G T C C C C A C C C A C C T T C T C G C C A C C C C C T G C C T C T C A C C C A A G G G G C A G A A T T A C T T T A G G A T G T A A 980
 981 A T T C T G T C A T T G C C T G G C T G C G C T C C T G G A G C A A A A G A G A A C T A A C C T C T T C C C C C T G G T T T C C C C 1050
 1051 T C A A C T G T C T G T G G C T G C A A A G G C A G A G G C A G G A T C A C C A G G T G A T G A C A A G T C C C A G C T T A C A A G G A 1120
 1121 G G A A A C T C A G G T C C A G A G A G A T G G A T T A T C C C A A A G C C C C A A C A T C C A G T T C T G C T G A A G A G G C G G T 1190
 1191 G G C A G G G T G G C A C G T G T G G G G A A G C C C A G G T C C T G C C T G C C T C T C A C C C T A A T G T C A T C C T C A C C C 1260
 1261 T C T C T C T C C C C C A C A G T G C T C A G G A G T A C T G A G A A G T C C T G G C T G A C A A C C T C T G T G T C C G C T T C T C 1330
 alleuArgArgTyr***
 106
 1331 C A A C G C C C C T C C C C T G C T C C C C T T C A A G C A A C T C C T G T T T T A T T A T G T A T T A T T T A T T A T T A T T 1400
 1401 T G G T G G T T G T A T A T A A G A C G G T T C T T A T T T G T G A C C A C A T T T T T C C A T G T G A A A T A A A G T C A A C A T T A 1470
 1471 G A G C T C T G T C T T T T G A A A A A A A A A A A A A A G G A A T T C 1507

FIG.3B

Mature Pig BNP cDNA (10-13-88)

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1  GAATTCAGGCTGCTAGGAAGTGAAGTGAACCTGGACCCAGCTCAGCGGCAGCAGCGGCAGCAGG 70
71  CAGCAGCCTCTATCCTCTCCTCCAGCCACATGGGCCCCCGGATGGCGCTTCCCGCGTCTCCTGCTCCT
    MetGlyProArgMetAlaLeuProArgValLeuLeuLeuLeu
141  GTTCTTGACACCTGTTGCTAGGATGCCGTTCCCATCCACTGGGTGGCGCTGGCCTGCCTCAGAACTG
    uPheLeuHisLeuLeuLeuGlyCysArgSerHisProLeuGlyGlyAlaGlyLeuAlaSerGluLeu
211  CCAGGGATACAGGAGCTGCTGGACCGCCTCGGAGACAGGCTCTCCGAGCTGCAGCGCGGAGCGGACGACC
    ProGlyIleGlnGluLeuLeuAspArgLeuArgAspArgValSerGluLeuGlnAlaGluArgThrAspL
280  TGGAGCCCTCCGGCAGGACCGTGGCCTCACAGAGCCTGGAGCGGAGGAGCAGCCCCACGGGGGT
    euGluProLeuArgGlnAspArgGlyLeuThrGluAlaTrpGluAlaArgGluAlaProThrGlyVa
350  TCCTGGGCCCCGAGTAGCATCTTCCAAGTCTCTCCGGGAATACGCAGCCCCAAGACGATGCGTGACTCT
    lLeuGlyProArgSerSerIlePheGlnValLeuArgGlyIleArgSerProLysThrMetArgAspSer
420  GGCTGCTTTGGGGGAGGCTGGACCGGATCGGCTCCCTCAGCGGCCCTGGGCTGCAATGTGCTCAGGAGGT
    GlyCysPheGlyArgArgLeuAspArgIleGlySerLeuSerGlyLeuGlyCysAsnValLeuArgArgT
490  ACTGAGAAGTCTGCTGACAACCTCTGTGTCGGCTTCTCCAACGCCCTCCCTGCTCCCTTCAAAGC
    yr***
560  AACTCCTGTTTTTATGTATTATTATTATTATTATTATTGTTGTTGTATATAAGACGGTTCTTATTT
630  GTGAGCACATTTTTTCCATGGTGAATAAAGTCAACATTAGAGCTCTGTCTTTTGAATAAAAAAAAAA
700  GGAATTC 707

```

FIG.4

FIG. 5A

FIG. 5A

771	CAGAGCTGCAGGCAGAGCAGTTGGCCCTGGAACCCCTGCACCGGAGCCACAGCCCCCGCAGAACCCCGGA	840
	erGluLeuGlnAlaGluGlnLeuAlaLeuGluProLeuHisArgSerHisSerProAlaGluAlaProGl	
841	GGCCGGAGGAACGCCCGTGGGGTCCTTGCACCCCATGACAGTGTCTCTCCAGGCCCTGAGAAGACTACGC	910
	uAlaGlyGlyThrProArgGlyValLeuAlaProHisAspSerValLeuGlnAlaLeuArgArgLeuArg	
911	AGCCCCAAGATGATGCACAAGTCAGGGTCTTTGGCCGGAGGCTGGACCGGATCGGCTCCCTCAGTGGCC	980
	SerProLysMetMetHisLysSerGlyCysPheGlyArgArgLeuAspArgIleGlySerLeuSerGlyL	
981	TGGGCTGCAATGGTAAGCCGCCCTCCCTGCGCGCCTTGGCTCCCCCTCCCCAGCCCCCTGGGTTGACCCCTT	1050
	euGlyCysAsnV	
1051	GGAACCCCTTCTGGGTTTGTGTCTCGGGGGATCACACTCTGAGGAAAGGACATCTGGACATCGCTCCTT	1120
1121	CTTGCTGACAGTCCTAAGGGCCCAAGGAGTACGTTTCTGGAATACTACGTGTGGACATCGTTGTCCAGGG	1190
1191	TCCCTACCCACCTCCTAGCCCCCTCCTGCTCTCGCACCCCAAGGGCAGAAATCATCTTAGGATGGAATCA	1260
1261	GTCGTTGTCTGGAAGCATCTCCTTGGAGCAGAAAGAGTCCTAAACATCGTCCTCGTAGCTCTCTGTCT	1330
1331	GTCTGTAGCCACGAAGGCAGAGTACAGGTCACCGGGCAGTGTATGCCAGTTAACAGAGGAGGAGA	1400
1401	CTGAGGCTCTAGAGAGATGGATTATTCCAAGCCTCAAACATCCAGATCGGCTGAGGTTGGGTGGC	1470
1471	AGGGATGGCTCCTGGGCTTGGGAAGCTCGGATCCTGCCTCAGTCTCCCACCTGACGCCATCATCCCCCTC	1540
1541	TCTCTCCTCCACAGTGTGAGAAAGTATTAAAGGAGGAAGTCCCAGTCCCACATCTGCATTGGATTCT	1610

FIG.5B

alleuArgLysTyr***

1611	TCAGCAGCCCTGAGCCCTTGGAAGCAGATCTTATTATTCGTATTATTATTATTATTATTTCGATTG	1680
1681	TTTTATATAAGATGATCCTGACGCCCGAGCACGGATTTCCACGGTGAAATAAAGTCAACCTTAGAGCTT	1750
1751	CITTTGAAACCGATTGTCTCCTGTGCATTAAAGTAACACATCATTTTAAAAAA	1804

FIG.5C

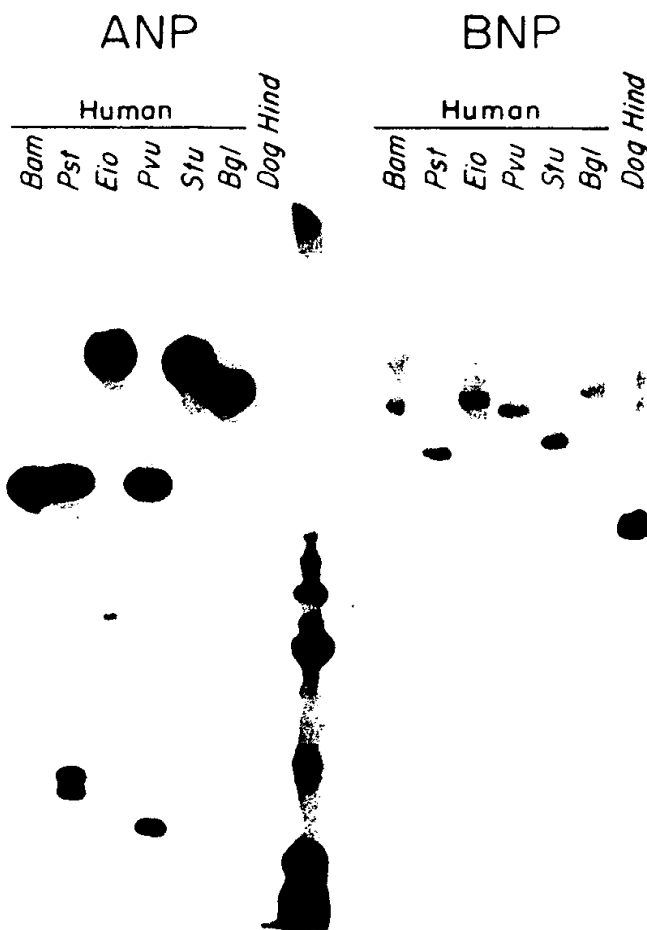


FIG.6

Human BNP Gene 12-12-88

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1  CCCACGGTGTCCTCCGAGGAGCCAGGAGGAGCACCCTCCGAGGCTGAGGGCAGGTGGGAAGCAACCCGGACG  70
71  CATCGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCCTCCGAGTCCCTCCAGAGACATGGATC  140
    MetAspP
141  CCCAGACAGCACCTTCCCGGGCGCTCCTGCTCCTGCTCTTCTTGCACTCTGGCTTTCTCTGGGAGTCTGTTT  210
    roGlnThrAlaProSerArgAlaLeuLeuLeuLeuPheLeuHisLeuAlaPheLeuGlyGlyArgSe
211  CCACCCGCTGGGAGCCCGGTTTCAGCCTCGGACTTGAACGTCCGGGTTACAGGTGAGAGCGGAGGGC  280
    rHisProLeuGlySerProGlySerAlaSerAspLeuGluThrSerGlyLeuGln
281  AGCTCAGGGGATTGGACAGCAGCAATGAAGGTCCTCACCTGTCTCCCAAGAGGCCCTCATCTTTCC  350
351  TTTGGAATTAGTGATAAAGGAATCAGAAATGGAGAGACTGGGTGCCCTGACCCTGTACCCCAAGGCAGTC  420
421  GGTTCACCTTGGTGCCATGAAGGGCTGCTGAGCCAGGGTGGGTCCCTGAGGCTTGGACGCCCCCATTC  490
491  TTGCAGGAGCAGCGCAACCATTTGCAGGGCAAACTGTCGGAGCTGCAGGTGGAGCAGACATCCCTGGAGC  560
    GluGlnArgAsnHisLeuGlnGlyLysLeuSerGluLeuGlnValGluGlnThrSerLeuGluP
561  CCCTCCAGAGAGCCCGCTCCACAGGTGTCTGGAAGTCCCGGAGGTAGCCACCGAGGGCATCCGTGG  630
    roLeuGlnGluSerProArgProThrGlyValTrpLysSerArgGluValAlaThrGluGlyIleArgG
631  GCACCGCAAAATGGTCTCTACACCCCTGGGGGCACCACGAAGCCCCAAGATGGTCAAGGGTCTGGCTGC  700
    yHisArgLysMetValLeuTyrThrLeuArgAlaProArgSerProLysMetValGlnGlySerGlyCys

```

FIG.7A

701 TTTGGAGGAAGATGACCGGATCAGCTCCTCCAGTGGCTGGCTGCAAAGTTAAGCACCCCTGCCAC 770
PheGlyArgLysMetAspArgIleSerSerSerGlyLeuGlyCysLysV

771 CCCGGCCGCCTTCCCCCATTCAGTGTGTGACACTGTTAGAGTCACCTTGGGGGTTTGTCTCTGGGAA 840

841 CCACACTCTTTGAGAAAAGTCACTGGACATCGCTTCCTCTTGTTAACAGCCTTCAGGGCCAAGGGTG 910

911 CCTTTGTGGAATTAGTAAATGTGGGCTTATTTCAATTACCATGCCCCACAATACCTTCTCCCCACCTCCTAC 980

981 TTCTTATCAAAGGGCAGAAATCTCCTTTGGGGTCTGTTTATCATTTGGCAGCCCCCAGTGGTGCAGAA 1050

1051 AGAGAACCAACATTTCTCCTGTTTCTCTAACTGTCTATAGTCTCAAAGGCAGAGCAGGATCAC 1120

1121 CAGAGCAATGATAATCCCCAATTTACAGATGAGGAAACTGAGGCTCAGAGAGTTGCATTAAAGCCTCAAAC 1190

1191 GTCTGATGACTAACAGGGTGGTGGTGGCACACGATGAGGTAAGCTCAGCCCCCTGCCTCCATCTCCCACC 1260

1261 CTAACCATCATCACCCCTCTCTCTTTCCCTGACAGTGCTGAGGGCGCATTAAGAGGAAGTCCTGGCTGCAG 1330
alLeuArgArgHis***

1331 ACACCTGCTTCTGATTCCACAAGGGGCTTTTTCCTCAACCCTGTGGCCCTCATCTTTCCTTTGGAATTAG 1400

1401 TGATAAGGAATCAGAAAATGGAGAGACTGGGTGCCCTGACCCCTGTACCCAAGGCAGTCGGTTCACCTTGG 1470

1471 GTGCCATGAAGGGCCTGGTGAGCCAGGGGTTGGGTCCCTGAGGCTTTTA 1519

FIG.7B

Pig PreproBNF
Dog PreproNRP
Human PreproNRP

[illegible]

FIG. 8